III. Remarks

A. Rejection Under 35 USC §112, 2nd ¶

Claims 10 and 11 stand rejected as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regards as the invention. The Examiner contends there is a lack of antecedent basis for "said sequentially administered doses. Applicants have amended the Claims for antecedent basis. This amendment is not narrowing and no estoppel should result from the amendment.

Literal support for the amendment, by sequential non-daily intermittent administration, can be found in the specification on page 4, line 5 where it is explained in lines 7-10 of that page that "sequential non-daily intermittent administration means that each administration is followed by a pause-period comprising at least one day on which no progestogen is administered, and said pause period is followed by another administration of anti-progestogen". Accordingly, antecedent basis has been found. Applicants respectfully request reconsideration of the rejection in light of this response.

B. Rejections Under 35 USC §103

Claims 2, 4, 10-14 and 16-18 stand rejected as being unpatentable over WO 93/21927 to Hodgen (hereinafter referred to as the '927 patent) in view of publication XP-002124156 to Schoonen et al (hereinafter referred to as the Schoonen publication) and US Pat No. 5,854,235 to Hamersma (hereinafter referred to as the '235 patent). The Examiner contends that the '927 patent teaches a method of minimizing menstrual bleeding irregularities in individuals using progestin-only pharmaceutical preparation, such as contraceptive, such as administering anti-progesterone such as

 The Examiner directs attention to the abstract, p. 5, ll. 20-30 and p.7, ll. 20-32. The Examiner further contends that the '927 patent teaches that the antiprogestin can be administered monthly, or at other intermittent levels, p.9, ll. 32-36. The Examiner further asserts that the '927 patent further teaches that a suitable regimen is an antiprogestin administered every 30 days, every 60 days or every 90 days and in the case of contraceptives, the antiprogestin can be administered on the 28th day of each cycle, p. 10, ll. 5-20.

The Examiner further asserts that the dosing schedule of Applicants' Claim 4 is obvious because it was convential. However, the Examiner provides no additional teachings from the art.

Applicants respectfully request reconsideration in light of this argument and well accepted case law.

It is basic patent law that to establish a prima facie case of obviousness, an Examiner must, inter alia, show "some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings of the references." ***In re Fine***, 837 F.2d 1071, 1074, 5 USPQ2d 1596, 1598 (Fed. Cir. 1988). "The motivation, suggestion or teaching may come explicitly from statements in the prior art, the knowledge of one of ordinary skill in the art, or, in some cases the nature of the problem to be solved." ***Kotzab***, 217 F.3d at 1370, 55 USPQ2d at 1317. Here, the Examiner has not identified the aspects of Applicants invention and is only combining what Applicants admit is prior art, but not what Applicants assert comprises their invention.

The Examiner contends to have identified, in the prior art, each individual part claimed. However, it has long been the law that this is insufficient to defeat patentability of the whole claimed invention. ***See id.*** Rather, to establish obviousness based on a combination of the

elements disclosed in the prior art, there must be some motivation, suggestion or teaching of the desirability of making the specific combination that was made by the applicant. ***See In re Dance***, 60 F.3d 1339, 1343, 48 USPQ2d 1635, 1637 (Fed. Cir. 1998); ***In re Gordon***, 733 F.2d 900, 902, 221 USPQ 1125, 1127 (Fed. Cir. 1984). Here, Applicants' invention is not depicted by the Examiner's cited prior art.

To begin, Applicants would like to point out that embodiments of the subject invention are directed to a method of anti-progestogen therapy by sequential non-daily intermittent administration of Org 33245. This is a selection invention. It is clear from the subject application that Org 33245 *"has a surprisingly better suitability than the others for being administered intermittently"* (see page 1, lines 19-20 of the specification). In addition, *"Org 33245 not only has a strong activity and high selectivity, but also a strong binding to human orosomucoid, which is indicative of a relatively long half life"* (page 3, lines 1-3 of the specification).

Moreover *"the excellent suitability of Org 33245 comes all the more as a surprise since this could not be expected from the closely related Org 33628.....* "(see specification, page 3, lines 8-16).

None of the references cited by the Examiner teach or suggest these surprising properties for Org 33245, which can be put to use in the claimed anti-progestogen therapy.

The Examiner contends that Hodgen teaches a method for minimizing menstrual bleeding irregularities in individuals using progestin-only pharmaceutical preparations, such as contraceptives comprising administering anti-progesterone such as Org 31710. The Examiner

further states that Hodgen teaches that the anti-progestin can be administered monthly, or at other intermittent intervals. The Examiner further contends that Hodgen teaches the intervals and numbers of doses can vary and a suitable regimen is having the anti-progestin administered every thirty days, every sixty days or every ninety days and in the case of contraception, the anti-progestin can be administered on the twenty-eight day of each cycle.

However, it cannot be disputed that Hodgen does not teach or suggest a method of anti-progestogen therapy by sequential non-daily intermittent administration of Org 33245. In fact, Hodgen does not mention Org 33245 at all, let alone intermittent administration of Org 33245. At best, the disclosure of Hodgen as a whole provides the skilled person with the understanding that the anti-progestogen is to be given once per treatment cycle (i.e. on the 28th or 30th day of the treatment) and not on a sequential non-daily intermittent basis. This becomes particularly apparent from page 9, line 33-35: *"....whereas the anti-progestin is administered monthly, or at other intermittent intervals."* This also is apparent from page 10, lines 9-13, which recite: *"The number of doses can vary from monthly to longer intervals... Thus, a suitable regimen is having the anti-progestin administered every thirty days, every sixty days or every ninety days."* (emphasis added). The present invention does not relate to a regimen wherein the anti-progestogen is administered once per month or once per two months, etc. but rather e.g. once per two days, but not every day.

The Examiner then contends that Schoonen compares the anti-progestinic activity of Org 33245 to that of Org 31710 and shows that org 33245 is more active. Applicants do not dispute that Schoonen *et. al.* illustrates that the activity of Org 33245 is higher than that of Org 31710. However, Schoonen *et. al.* further illustrates that the activity of Org 33628 is higher than that of

Org 33245.

The Examiner then contends that Hamersma et al. teaches that Org 33245 is useful in contraception and exhibits the normal activities for anti-progestogen such as treatment of menstrual disorders and hormone dependent tumors. Applicants agree that Hamersma et al. discloses that Org 33245 is useful in contraception and exhibits the normal activities for an anti-progestogen, such as treatment of menstrual disorders and hormone dependent tumors. Hamersma et al. does not teach specific methods of anti-progestogen therapy using Org 33245 or any other progestogen.

The Examiner concludes that it would have been obvious to one of ordinary skill in the art to modify Hodgen's method to employ Org 33245 in place of Org 31710 because Schoonen teaches that Org 33245 is more active than Org 31710 and because Hamersma et al. teach that Org 33245 exhibits normal activities known for anti-progestogen such as treatment of menstrual disorder and usefulness for contraception. The Examiner further contends that one of ordinary skill in the art would have been motivated to modify Hodgen's method to employ Org 33245 in place of Org 31710 to achieve expected benefit of increased activity of anti-progestin therapy for contraception and a decrease in menstrual bleeding. The Examiner states that absent any evidence to the contrary, there would have been reasonable expectation of successfully employing Org 33245 in Hodgen's method. Applicants respectfully request reconsideration in light of this response.

Applicants assert that there is no motivation in Hodgen to employ Org 33245 in place of Org 31710. Hodgen merely lists a number of anti-progestogens (page 7, lines 20-31) but does not teach or suggest that certain anti-progestogens are better suited for particular anti-

progestogen therapy regimes than others.

Schoonen et al.does not supply the teaching. Even though Schoonen et al. teaches that Org 33245 has a better activity than Org 31710, it also teaches that Org 33628 has a better activity than Org 33245. Therefore, taking the line of reasoning of the Examiner, there may have been motivation to pick Org 33628 for the subject anti-progestogen therapy because it was more active than both Org 31710 and Org 33245; but there was surely no motivation to elect Org 33245 since (i) according to Schoonen et al. Org 33245 was less active than Org 33628 and (ii) Org 33628 was in fact mentioned in the list of anti-progestogens present in Hodgen whereas Org 33245 was not.

Surprisingly however (as also explained in detail above and in the application's specification) the present application demonstrates that Org 33245 is better suited for embodiments of the present invention than Org 33628, even though it would have been expected in the art, from the Scoonen *et al.* teaching, that Org 33628 would be better suited: *"the excellent suitability of Org 33245 comes all the more as a surprise since this could not be expected from the closely related Org 33628 which, in fact, has been proposed for use in the regimens described in EP 549041 and EP 582338. Org 33628, although being highly advantageous from the perspective of cost-price and activity, suffers from a drawback particularly associated with intermittent use. This drawback is its relatively rapid metabolism, as can be seen from the short half-life in humans (about 12 hours). This confronts the person skilled in the art with the problem of finding an alternative which has the advantages of Org 33628, but does not have this drawback. The invention obviates this drawback and provides the use of Org 33245...* "(see specification, page 3, lines 8-16). Accordingly, this is a surprising and unexpected result.

Further, the lack of motivation in Hodgen to use Org 33245 in the subject method of anti-progestogen therapy is also not remedied by Hamersma et al. which does not describe any particular regimen at all, let alone which compound would be better in which regimen. The limitations of Applicants' invention are not disclosed or taught.

Furthermore, the rejection of Claim 4 is incorrect because the Examiner has not identified the elements of the Claim in the prior art. Rarely will the skill in the art component operate to supply missing knowledge or prior art to reach an obviousness judgment. ***See W.L. Gore & Assocs., Inc. v. Garlock, Inc.*** ,721 F.2d 1540, 1553, 220 USPQ 303, 312-13 (Fed.Cir.1983) ("To imbue one of ordinary skill in the art with knowledge of the invention in suit, when no prior art reference or references of record convey or suggest that knowledge, is to fall victim to the insidious effect of a hindsight syndrome wherein that which only the inventor taught is used against its teacher."). Skill in the art does not act as a bridge over gaps in substantive presentation of an obviousness case, but instead supplies the primary guarantee of objectivity in the process. ***See Ryko Mfg. Co. v. Nu-Star, Inc.***, 950 F.2d 714, 718, 21 USPQ2d 1053, 1057 (Fed. Cir.1991). The Examiner has not even identified all aspects of Applicants' invention in the prior art. In rejecting Claim 4, the Examiner has stated that a dosing schedule of four (4) days would have been obvious. This is not an identification of the elements. Accordingly, Applicants respectfully request reconsideration of the rejection.

Further, Claim 11 is patentable over the cited prior art as detailed above. Claim 4 is dependent on claim 11 and is thus also patentable over the art cited. As well, Applicants do not understand the basis of the remark of the Examiner that "1-7 days during a cycle of 28-32 day

administration is obvious since this is within the conventional dosing regimens of contraception". There is no such thing as a conventional dosing regimen for contraception. This is because the contents of a contraceptive must be able to cause contraception, i.e. prevention of pregnancy. For example, just a bottle containing tablets or pills could not possibly cause contraception. This is because contraception does not just consist of a bottle of tablets (like a bottle of vitamins!). Contraception comprises a collection of daily dosage units which is composed of such numbers to be taken within a particular amount of time and provided in such an order that the administration of the dosage units in the prescribed order and the prescribed time will actually lead to contraceptive protection.

In summation, none of the cited references, either alone or in combination teach or suggest the method of anti-progestogen therapy as claimed and disclosed in the subject application. Accordingly, Applicants respectfully request reconsideration of the rejection in light of this response.

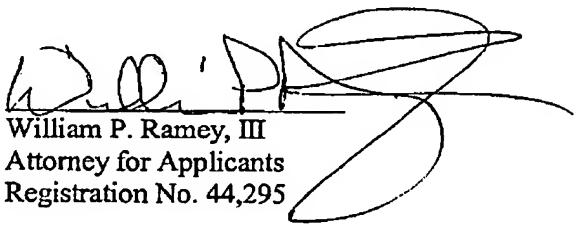
Obviousness is a question of law based on findings of underlying facts relating to the prior art, the skill of the artisan, and objective considerations. ***See*** ***Graham v. John Deere Co.*** , 383 U.S. 1, 17, 148 USPQ 459, 467 (1966). A determination of obviousness can not be based on the hindsight combination of components selectively culled and created from the prior art to fit the parameters of the patented invention. There must be a teaching or suggestion within the prior art, or within the general knowledge of a person of ordinary skill in the field of the invention, to look to particular sources of information, to select particular elements, and to combine them in the way they were combined by the inventor. ***See*** ***Heidelberger***

Druckmaschinen AG v. Hantscho Commercial Prods., Inc., 21 F.3d 1068, 1072, 30 USPQ2d 1377, 1379 (Fed. Cir. 1994). Here, the elements of Applicants invention have not been disclosed in the cited prior art, the citcd prior art teaches away from Applicants' invention, and Applicants' invention demonstrates surprising results that are unexpected from the teaching of the prior art. Accordingly, Applicant respectfully request reconsideration of the rejection.

IV. Conclusion

Applicants respectfully request reconsideration of the rejection in light of the amendments and argument. The Claims are believed in a condition for allowance and such action is requested. Applicants respectfully request the Examiner contact the undersigned attorney to facilitate allowance of the case. Please charge any required fees and credit any credits to deposit account 02-2334.

Respectfully submitted,



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